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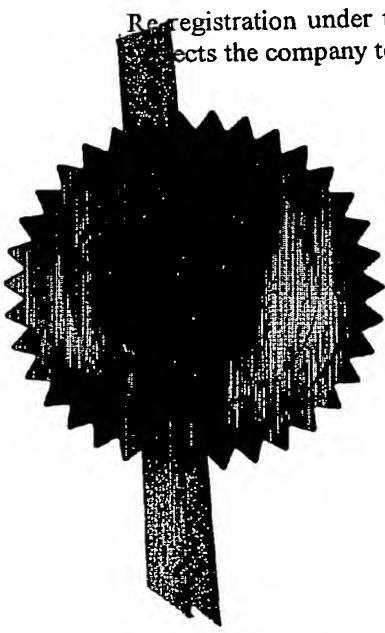
I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

I also certify that the application is now proceeding in the name as identified herein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

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Signed

Dated 28 August 2003

An Executive Agency of the Department of Trade and Industry

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GB0215876.4

By virtue of a direction under Section 32 of the Patents Act 1977, the application is proceeding
in the name of,

E2V TECHNOLOGIES LIMITED,
Incorporated in the United Kingdom,
106 Waterhouse Lane,
CHELMSFORD,
Essex,
CM1 2QU,
United Kingdom

[ADP No. 08457749001]

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THE PATENT OFFICE	
Patents Form 1/77	10 JUL 2002
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Patents Act 1977
(Rule 16)

1/77

Request for grant of a patent
(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form.)

The Patent Office

 Cardiff Road
 Newport
 South Wales
 NP9 1RH

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1. Your reference	45793 1763758.GBA/15D	1763758.GBA/15D	
2. Patent application number <i>(The Patent Office will fill in this part)</i>	0215876.4	0215876.4	
3. Full name, address and postcode of the or of each applicant <i>(underline all surnames)</i>	Marconi Applied Technologies Limited One Brunton Street London W1X 8AG		
Patents ADP number <i>(if you know it)</i>	7803513001		
If the applicant is a corporate body, give the Country/state of its incorporation	United Kingdom		
4. Title of the invention	SPECTROSCOPY METHODS AND DEVICES		
5. Name of your agent <i>(if you have one)</i>	N. Hucker Reddie & Green Marconi Intellectual Property 16 Theobalds Marrable House Road The Vineyards Great Baddow Chelmsford Essex CM2 7DS		
Address for service in the United Kingdom to which all correspondence should be sent <i>(including the postcode)</i>	London WC1X 8EC		
Patents ADP number <i>(if you know it)</i>	8225245001		
6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and <i>(if you know it)</i> the or each application number	Country	Priority application number <i>(if you know)</i>	Date of filing <i>(day / month / year)</i>
7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application		Date of filing <i>(day / month / year)</i>

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*
- any applicant named in part 3 is not an inventor, or*
 - there is an inventor who is not named as an applicant, or*
 - any named applicant is a corporate body.*
- See note (d)*

YES

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form.
Do not count copies of the same document.

Continuation sheets of this form	(0)
Description	3
Claim(s)	(0)
Abstract	(0)
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10. If you are also filing any of the following, state how many against each item.

Priority documents	(0)
Translations of priority documents	(0)
Statement of inventorship and right to grant of a patent (Patents Form 1/77)	(0)
Request for preliminary examination and search (Patents Form 9/77)	(0)
Request for substantive examination (Patents Form 10/77)	(0)
Any other documents (please specify)	

I/We request the grant of a patent on the basis of this application.

11.

Signature Nerys Hucker Date 10/07/02

12. Name and daytime telephone number of person to contact in the United Kingdom

Nerys Hucker
01245 493 493 ext.3122

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After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Surface Plasmon Absorbance Raman Spectroscopy

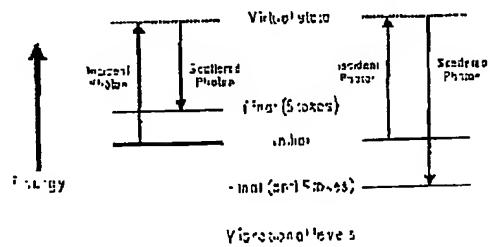
Patent Concept Document

Richard Gilbert

June 25, 2002

Background

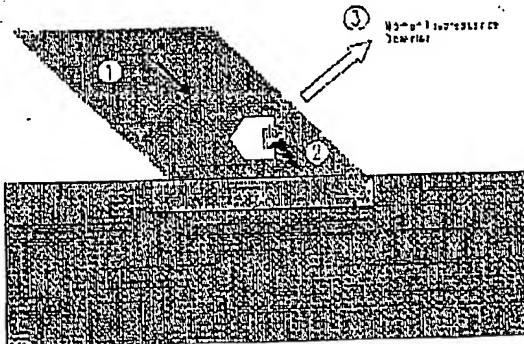
When light is scattered from a molecule, most of the photons are elastically scattered. The majority of the scattered photons have the same energy (frequency) and wavelength as the incident photons. However, a small fraction of the light (approximately 1 in 10^7 photons) is scattered at frequencies different from, and usually lower than, the frequency of the incident photons (see figure, below). When the scattered photon loses energy to the molecule, it has a longer wavelength than the incident photon (termed Stokes scatter). Conversely, when it gains energy, it has a higher wavelength (termed anti-Stokes scatter).



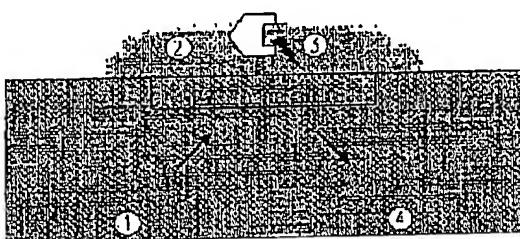
The process leading to this inelastic scatter is termed the Raman effect (after Sir C.V.Raman, who discovered it in 1928), and is associated with a change in the vibrational, rotational or electronic energy of the molecule. Energy transferred from the photon to the molecule is usually dissipated as heat. Similarly, it is possible for thermal energy to be transferred to the scattered photon, thus decreasing its wavelength. In classical terms, this interaction can be viewed as a perturbation of the

molecule's electric field, which is dependent not just on the specific chemical structure of the molecule, but also on its exact conformation and environment. The energy difference between the incident photon and the Raman scattered photon is equal to the energy of a vibrational state of the scattering molecule. A plot of the intensity of the scattered light versus the energy difference (wavelength) is termed the Raman spectrum [RS].

The Raman scattering from a compound or ion within a few Angstroms of a structured metal surface can be 10^3 to $10^5 \times$ greater than in solution. This surface-enhanced Raman scattering [SERS] is strongest on silver, but is readily observable on gold and copper as well. Recent studies have shown that a variety of transition metals may also give useful SERS enhancements. The SERS effect is essentially a quenching of fluorescence caused by energy transfer between the molecule and an electromagnetic field near the surface of the metal (see figure, right). The electric vector of the excitation laser \odot induces a dipole in the surface of the metal. The restoring forces from the positive polarisation charge result in an oscillating electromagnetic field at a resonant frequency of this excitation. In the Rayleigh limit, this resonance is determined mainly by the density of free electrons at the surface of the metal (the 'plasmons') determining the so-called 'plasma wavelength', as well as by the dielectric constants of the metal and its environment.



Molecules adsorbed or in close proximity to the surface experience an exceptionally large electromagnetic field in which vibrational modes normal to the surface are most strongly enhanced. This is the surface plasmon resonance [SPR] effect which enables a through-space energy transfer between the plasmons and the molecules near the surface Θ . Scattered photons may then be measured using conventional spectroscopic detectors Θ . The intensity of the surface plasmon resonance is dependent on many factors including the wavelength of the incident light and the morphology of the metal surface, since the wavelength should match the plasma wavelength of the metal. SPR can be performed using colloidal metal particles, or thin metal films. For a 5μm silver particle the plasma wavelength is about 382nm, but it can be as high as 600nm for larger ellipsoidal silver particles. The plasma wavelength is to the red of 650nm for copper and gold particles, the other two metals which show SERS at wavelengths in the 350-1000nm region. The best morphology for surface plasmon resonance excitation is a small (<100nm) particle or an atomically rough surface on a thin (*ca.* 50nm) metal film.



The SPR effect is also used as an analytical technique in its own right (see figure, left). An excitation laser Θ is arranged so that it impinges on the metal surface at an angle close to the critical angle (determined by the refractive index of the metal). The SPR effect causes an 'evanescent wave' Θ , an electromagnetic field which extends approximately 400nm from the metal surface. Energy transfer Θ between this field and the analyte molecule(s) results in a change in the

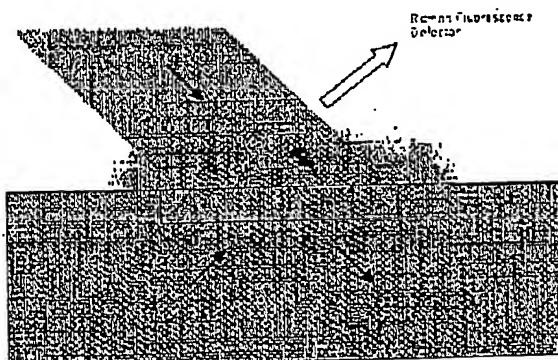
intensity of refracted light Θ , which can be detected using conventional spectroscopic devices.

Both RS and SPR are powerful techniques which are routinely used to follow molecular interactions or quantify molecules at extremely low concentrations. This invention describes a way to combine the two techniques to allow the simultaneous measurement of the RS and SPR effects, and to selectively enhance the interaction between the surface plasmons and the analyte molecules. It also describes the incorporation of detectors for both effects onto a lab-on-a-chip scale device.

The Idea

It is possible to combine both RS and SPR technologies into a single detector (see figure, right). The two detector systems can operate independently, giving discrete or simultaneous measurements of the same analyte sample. However, they can also be used synergistically, which is the key invention of this patent proposal.

The efficiency of energy transfer between the molecular system and the plasmon field is dependent upon a match between the vibrational energy states of the molecule, and the quantum energy states of the surface plasmons. The former is determined by the molecular structure and environment, and the latter by the wavelength of the excitation laser and the composition and geometry of the metal particle or layer. This means that the SPR wavelength is tunable, either by controlling the excitation wavelength (e.g. by using a digitally-tunable diode laser) or the



composition and thickness of the metal layer. The SPR effect can therefore be selectively optimised to maximise the SERS signal from a particular analyte molecule. The benefits of this are that the strength of the SERS signal can be substantially increased for a given molecule (enabling a more sensitive detection), and that the SPR field can be adjusted to selectively enhance the signal from particular components of complex biological mixtures. Since the combined detector uses an artificial SPR field to absorb the fluorescence from the analyte molecules, I propose giving it the acronym SPARS, for surface plasmon absorbance Raman spectroscopy.

For a lab-on-a-chip device, there is the additional possibility of controlling the exact composition of the metal layer. Modifying the metal surface with a variety of dopant atoms would provide an additional means of modulating the plasma wavelength, maybe even resulting in an electronically-controllable SPR field.

The RS and SPR components can be physically separated, with the RS laser and detector arranged 'above' the analyte molecules, and the SPR laser and detector arranged 'below' them. The benefit of this for a lab-on-a-chip application is that it provides modularity: detectors can be built in all three combinations (RS only, SPR only, and SPARS) using the same basic components.

It may even be possible to extend the idea to allow three simultaneous detector technologies to be incorporated into the same device. If the metal film is etched appropriately (and deposited on a suitable piezoelectric substrate, such as quartz), it could be formed into a surface acoustic wave [SAW] delay line. Since a SAW device operates using completely different physical principles to the optical RS and SPR devices, it should not interfere in any way with their signals.

The SPARS detector, if it can be demonstrated to work, therefore offers the exciting possibility of developing a modular, multi-purpose lab-on-a-chip detector system which would enable the simultaneous collection of data based on several different physical principles. This would be a novel invention giving Micth a substantial advantage over our competitors.

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